Importance of left atrial volume index in the prediction of coronary artery disease in patients with abnormal Dobutamine stress echocardiography

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Abstract*:* Objective: Mortality post-acute myocardial infarction (MI) can be expected by applying Left atrial volume index (LAVI) but the predictive intensity of LAVI dilatation degrees has not been documented in adults with coronary artery disease (CAD). So we aim to evaluate the predictive value of left atrial volume index for Dobutaminestress echocardiographic abnormalities in patients with suspected CAD. **Patients and methods***:* 30 patients complaining of chest pain, suspected CAD were enrolled. LAVI was calculated at rest by biplane area length method and indexed to body surface area Dobutamine stress echocardiography (DSE) was done for all patients for detection of ischemia. and the results were confirmed by coronary angiography which is the gold standard for diagnosis of ischemia. **Results:** Patients with abnormal LAVI were significantly older, while it was not significantly related to gender. Diabetes and hypertension were the most prevalent risk factors in patients with high LAVI(68.75%, 58.34% respectively) followed by smoking, dyslipidemia and obesity. DSE was positive in 15 patient (93.75%)who have high LAVI., Patients with high LAVI > 28 ml/$m^2$was 16 patients, 15 of them showed positive coronary angiography. Conclusion: LAVI is a very valuable, readily available and practical way of screening for low risk IHD patients, and should be implemented as part of work-up for the diagnosis of IHD.
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1. Introduction:

One of the top of causes of morbidity and mortality worldwide is an ischemic heart disease (IHD) [(1).]

Echocardiography are used routinely for assessment of ejection fraction (EF) of left ventricle (LV), which used for prediction cardiovascular consequences [(2)], It was suggested that the dilatation of the left atrium (LA) is an indicator for diastolic disorder and used as a good predictor of cardiovascular results such as atrial fibrillation, stroke, heart failure (HF), and death. [(3)]

Measurement of the size of the left atrium is essential for supply with important prognostic in different patient populations and can be used as an indicator of cardiovascular risk disease[(4-6).]

Some authors found that measurement of the left atrial volume (LAV) may be a best index than of left atrial size [(7)].

Many investigators suggesting that the elevation in the LAVI can be used for expectation of mortality post MI, however the predictive influence of degrees of dilatation of LAVI has not been well-known in the often met clinical setting of ambulatory adults with CAD [(10, 11).]

Previous investigations maximized the normal value of LAVI for the expectation of risks affecting general cardiovascular system [(12-16)] and also the value of using a normal stress test for the expectation of low ischemic hazard [(17, 18).]

Therefore, the aim of the current work was to assess the predictive value of left atrial volume index for Dobutamine stress echocardiographic abnormalities in patients with known or suspected CAD.

2. Patients and Methods:

This study was done in cardiovascular department, Tanta University Hospital, from April 2016 to December 2016.

It was conducted on 30 patients complaining of chest pain (either typical or atypical), with one or more risk factors for CAD, Age ≥18 years. Good acoustic window, with good echogenicity.

Otherwise Patients with significant valve disease, Especially Mitral valve disease, Congenital heart disease (Large shunts), Atrial flutter and fibrillation, Bundle branch block And Poor acoustic window were excluded from the study.

The following clinical and demographic parameters were recorded; age, sex, hypertension, diabetes mellitus, hypercholesterolemia, Obesity **(**defined as Body Mass Index ≥ 30 Kg/m2), Current cigarette smoking was defined as active smoking within the past 12 months. Coronary artery disease was obtained by history or previous medical records.

12 lead ECG was done followed by transthoracic echocardiography for all study population.

Echocardiographic examination:

All study subjects underwent a complete echocardiographic study, including two-dimensional (2D), colour- flow Doppler, as well as tissue Doppler imaging (TDI) using machine vivid 7–dimension (GE Vingmed, Horten, Norway) all acquisitions were performed with a broad band M4s transducer. Imaging was performed in the standard para-sternal views and apical views with the patient in the left lateral position. Two dimensional, M-mode, Doppler echocardiography measurements and quantification were performed according to recommendations of the American Society of Echocardiography.

Left ventricular segmental wall abnormalities was documented at rest,

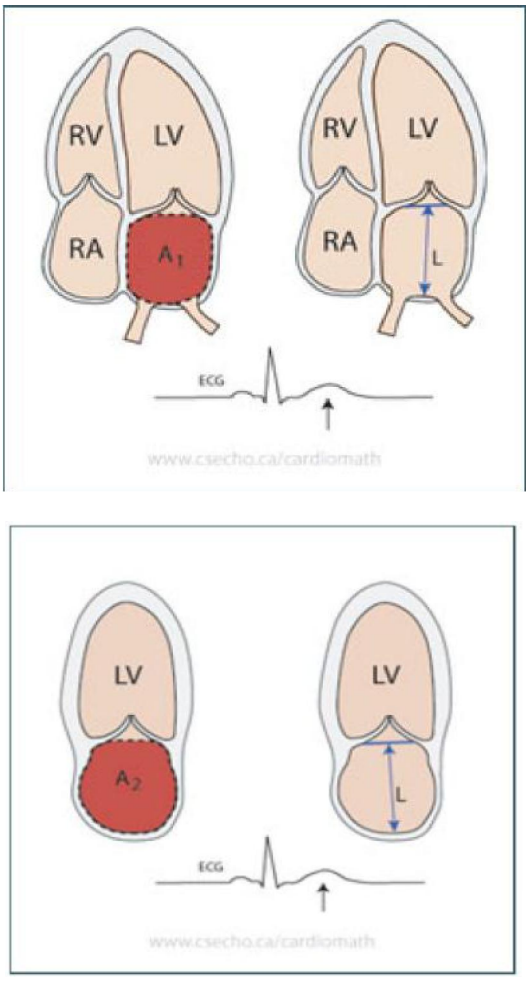

Figure (1): assessment of LAV. By biplane area length method.

LA size was measured at rest at the end-ventricular systole just preceding the mitral valve opening or at the end of the T wave on ECG (maximum LA size). And was calculated using biplane area length method in apical 4 chambers, and apical 2 champer views. and was indexed to body surface area for calculation of left atial volume index. As shown in figure 1.

A1 Max. planimetered LA area in apical 4-chamber (A4C) view

A2 Max. planimetered LA area in apical 2-chamber (A2C) view

L Length measured from back wall to line across mitral valve hinge points (cm)[19]

$$LAVolume = \frac{8}{3\pi} \times \frac{A1 \times A2}{L}$$

$$LAVI = \frac{LAVolume}{Bodysurfacearea}$$

Dobutamine stress echocardiography:

Dobutamine echocardiography was done for all patients to diagnose ischemic heart disease.

Begin dobutamine infusion at 5 µg/kg per minute. And increase dobutamine infusion every 3 minutes to maximum of peak dose 40 µg/kg per minute with atropine. segmental wall motion abnormalities were documented (as shown in figure (2).

Test was stopped due to either

I. Target heart rate (85% of age-predicted maximal heart rate or, if soon after myocardial infarction, 70% of age-predicted maximal heart rate).

II. Development of new regional wall motion abnormalities of at least moderate severity Peak dose.

III. Ventricular tachycardia or sustained supraventricular tachycardia.

IV. Severe hypertension (systolic blood pressure >220 mm Hg or diastolic blood pressure >110 mm Hg).

V. Substantial decrease in systolic blood pressure (a decrease of 20 mm Hg from previous level of infusion may be used as a guideline for terminating the test, but amount depends on baseline blood pressure and judgment of person monitoring the test).

VI. Intolerable symptoms.

Coronary Angiography:-

Coronary angiography was done for all the selected patients as a gold standard for ischemic heart disease, to confirm the results of Dobutamine stress Echocardiography.

Angiographic images were obtained from a femoral approach according to standard techniques, and were qualitatively analyzed for clinical purposes. A luminal diameter reduction >50% was considered a significant stenosis. The analyzed vessels included main coronary arteries (i.e. left main stem, left anterior

descending, left circumflex, and right coronary arteries) and secondary branches.

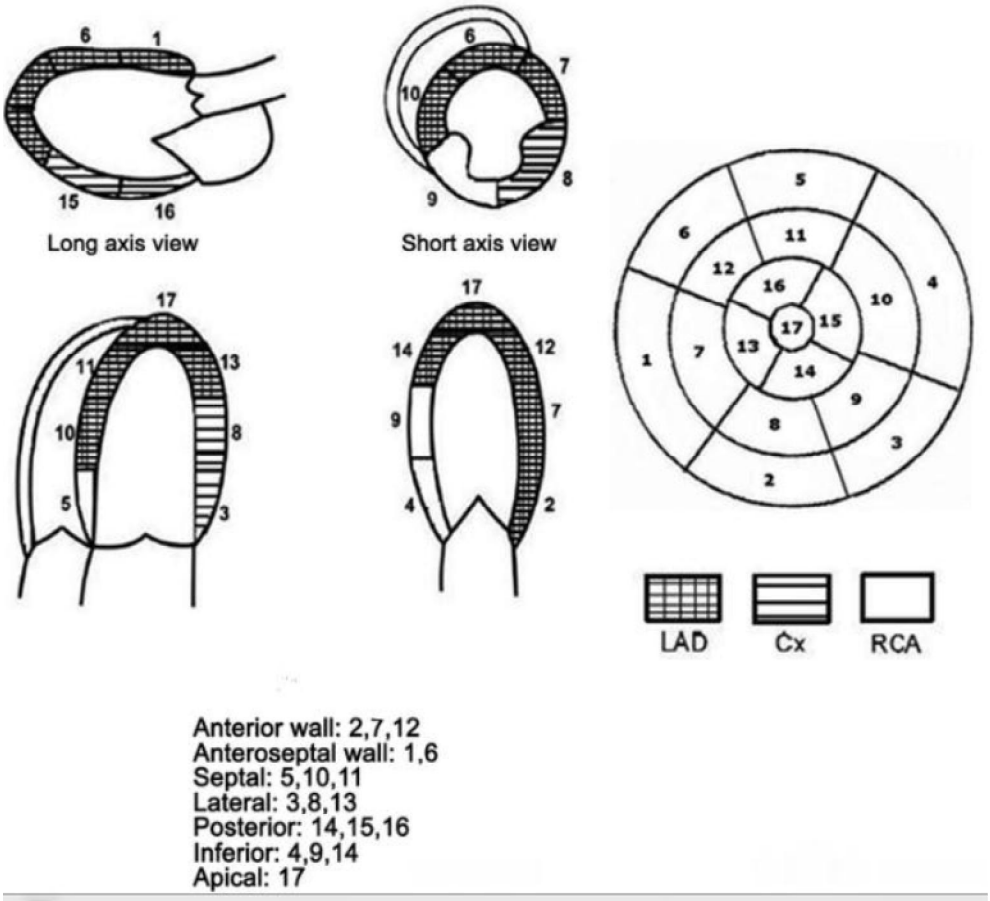

Figure (2):Left ventricular (LV) myocardial segmentation for echocardiographic wall motion analysis with corresponding distribution of coronary arterial blood supply, showing segmental distribution of the seven LV walls in dobutamine echocardiography
Cx = circumflex artery; LAD = left anterior descending coronary artery; RCA = right coronary artery. [20]

Statistical Analysis:

The collected data were organized, tabulated and statistically analyzed using SPSS version 19 (Statistical Package for Social Studies) created by IBM, Illinois, Chicago, USA. For numerical values the range mean and standard deviations were calculated. The differences between mean of the two studied groups were tested using Mann-Whitney test due to small sample size of groups which violate the guarantee for normal distribution of the variables. For categorical variable the number and percentage were calculated and differences between subcategories were tested by Fisher and Monte Carlo exact testes. The relations between two variables were tested by Pearson's, correlation coefficient. $P<0.05$ was considered statistically significant.

3. Results

The study included thirty patients who referred to cardiology department Tanta university hospital for clinical evaluation of myocardial ischemia and were classified according to LAVI into two groups:-

Group A (number = 14 patients):-patients with normal LAVI ≤ 28 ml /m^2.

Group B (number = 16 patients): patients with large LAVI **>** 28 ml /m^2

Demographic data were collected and reveal Male patients were 17 (56.67 %) of study population, otherwise female were only 13 (43.33%), with No significant difference of LAVI as regarding gender between two groups.

Age of study population ranged from 40 to 70 years old, with a mean of 57 years old. Patients with large LAVI were significantly older.

Risk factors for coronary artery disease were assessed in study populations, including hypertension, diabetes mellitus, dyslipidemia, smoking and obesity, Regarding risk factors, Diabetes mellitus was the most prevalnt risk factor in the group B (LAVI >28 ml

/m^2)with significantly statistical differenceamong both groups.

Otherwize, hypertension, dyslipidemia, smoking and obesity showed statistically non significant difference in LAVI among both groups. table (1)

Table (1): Relation of LAVI to risk factors of coronary artery disease

	Group A (14 pt)		Group B (16 pt)		P
	NO	%	NO	%	
HTN					
Yes	10	41.66%	14	58.34%	0.747
No	4	66.66%	2	33.34%	
Diabetes					
Yes	5	31.25%	11	68.75%	**0.006**
no	9	64.28%	5	35.72%	*
Dyslipidemia					
Yes	3	27.27%	8	72.73%	0.358
No	11	57.89%	8	42.11%	
Smoking					0.409
Yes	7	41.17%	10	58.83%	
No	7	53.84%	6	46.16%	
Obesity					
Yes	6	60%	4	40%	0.634
No	8	40%	12	60%	

Resting ECG changes in the form of dynamic symmetrical T wave inversion or slight ST depression was documented which is suggestive of ischemia. ECG changes suggestive of ischemia is statistically significant in patient with high (LAVI> 28 ml / m^2).

Dobutamine stress echocardiography was positive in 2 patients in group A (14.28%) Who had normal LAVI. and positive in 15 patient in group B (93.75%) who have high LAVI.

While DSE was negative in 12 patients in group A (85.72%), and in 1 patient in group B (6.25%).

All patients underwent coronary angiography as a gold standard for ischemic heart diseases. Patients with high LAVI > 28 ml/m^2 was 16 patient, 15 of them showed positive coronary catheterization.

P value was statistically calculated and showed significant change of LAVI in relation of coronary angiographic results, figure (3).

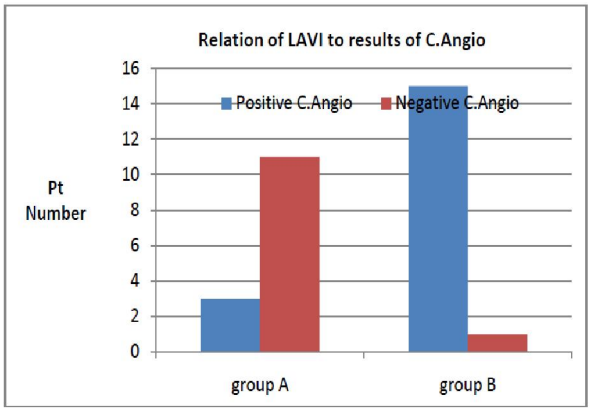

Figure (3): relation of LAVI to results of coronary angiography

Relation between results of DSE and coronary angiography as seen in table (2).

Table (2): Relation of results of DSE and coronary angiographic results between two groups

	Group A normal LAVI	Group B large LAVI
DES/Angio +ve+ve	2	15
DES/Angio +ve-ve	0	0
DES/Angio -ve+ve	1	0
DES/Angio -ve-ve	11	1

DSE: dobutamine stress echocardiography, Angio: coronary angiography.

The sensitivity, specificity and diagnostic accuracy of LAVI in the prediction of CAD compared to gold standard invasive coronary angiography was calculated as shown in table (3).

Table (3): Sensitivity, specificity, NPV, PPV and accuracy of LAVI in detecting ischemia

Sensitivity	specificity	Ppv	Npv	Accuracy
83.33%	91.66%	93.75%	78.57%	60%

NPV: negative predictive value, PPV: positive predictive value

4. Discussion:

Worldwide, ischemic heart disease is still the first cause of morbidity and mortality [(1)].

Change in the diastolic function is one of the early hemodynamic manifestations in patients with myocardial ischemia, which subsequently might event ually lead to inducing of chronic pressure to the left auricle secondary to increased left ventricular filling pressure [(21-23)].

The increase in the extent of LAVI may be attributed to chronic effectors and load of decreasing myocardial compliance and rising in filling pressure [(5)]**.** Increased left ventricular filling pressure causes increase in myocyte stretch and atrial wall pressure which induce rupture in the myocardium, lysis of myocytes, apoptosis and finally fibrosis resulting in dilatation of atrium [(24, 25)]**.** Measurement of left atrial size can be precisely determined through counting of left atrial volume [(7,26)]. In addition, measurement of left atrial volume with regarding to the body surface area (LAVI) has been connected with general cardiovascular risk liability and can supply with additional prognostic data about the usual coronary hazard factors in diverse patients residents [(5,6,13,14)]**.**

The diagnostic and predictive assessment of subjects with doubted ischemic heart disease (IHD) can be diagnosed by using DSE technique [(27-29)]**.** Normal LAVI during rest are accompanied with normal stress echocardiography result, proposing that this easy and readily available technique can be of value in identifying patients with low probability of ischemic heart disease [(30)]**.**

In several clinical medical services, stress testing may be not accessible, while it is frequently probable to get an echocardiographic imaging which comprises LAVI measurement. Since the LAVI has been strongly correlated with the result of DSE test, it can be considered as an indicator of a myocardial ischemia [(30)].

In the present study, we evaluated 30 patients of all who were referred to cardiology department Tanta university stress echocardiography unit to undergo routine DSE for investigation of IHD.

Our study aimed to evaluate the predictive value of LAVI in patients with suspected CAD.

Our patients were divided according to the resting LAVI values into two groups:

Group A consist of 14 patients with normal LAVI value (≤ 28 ml/m2).

Group B consist of 16 patients with high LAVI value (>28ml/m2).

Patients with abnormal LAVI were significantly older, while it was not significantly related to gender.

Regarding risk factors for CAD, diabetes and hypertension were the most prevalent risk factors in patients with high LAVI followed by smoking, dyslipidemia and obesity.

These results coincide with the results of **Andrea et al** [(31)], who studied 1480 healthy individuals, within two years duration to investigate clinical and echocardiographic correlates and found significant correlation of LAVI to age, BSA, diastolic function, and LV dimensions, with lesser extent to gender. **Patel et al** [(32)] who studied on 86147 for three years and found significant increase of LAVI in older patients.

As regard significantly higher LAVI in diabetic patients, this finding agree with **Kadappu et al** [(33)]. They evaluated volume and function of left atrium by counting strain and strain rate in 73 diabetic patients compared with age and gender matching control group. They found that high LAVI in diabetic patient is independent association of hypertension and even in patients with normal diastolic function. **Poulsen et al.** [(34)]also demonstrated high LAVI in diabetic patients, where it averaged about 1/3 of 305 patients suffering from diabetes mellitus.

These observations are also similar to that reported by **Wei et al.** [(35)]. In that study, suggested that in diabetic patients, alteration in LA may reflect on the left ventricle and leads to changes in LV diastolic function. Accordingly, diabetic patients complaining from an independent atrial cardiomyopathy may lead to causing enlargement in the LA.

As regard resting ECG changes, patients in the second group with high LAVI were significantly having baseline ECG changes.

No one in the first group has resting ECG changes, while in the second group six patients have resting ECG changes and ten patients with normal resting ECG.

In the same line with us, **Assiri et al** [36], who studied on Ninety consecutive patients who underwent DSE for suspected IHD in Saudia Arabia, within two years duration, and showed significant relation between ischemic ECG abnormalities and LAVI.

In order to screen for coronary artery disease, DSE was done. In the first group of patients with normal LAVI only two patients (11.76%) have positive test and 12 patients (92.31%) have negative test for induction of myocardial ischemia. in the second group of patients with abnormal LAVI, fifteen patients (88.24%) were positive and only one patient (7.69) was negative dobutamine stress test.

Our study coincide with, **Assiri et al** [36], who studied on ninety patient within two years duration and concluded that LAVI is a very valuable, readily available and practical way of screening for low risk IHD patients. In many centers, the sophisticated stress echocardiography tests might not be readily available, and hence LAVI, a procedure we strongly recommend, should be implemented as part of work-up for the diagnosis of IHD.

Also in the study of **Alsaileek et al** [30] on one hundred eighty randomly selected outpatient underwent DSE or exercise for suspected or known disease of the coronary arteries. They concluded that normal resting LAVI is easy tool of detecting individuals with low ischemic risk and can be predict precisely a normal stress echocardiograghy, which was the same finding of this study.

The finding of our study was the same with the study of Abdel-salam et al. [37] who measured LAVI at rest and peak DSE to separate those with multivessel CAD and to detect subjects complaining from coronary artery disease (CAD). They participated 100 subjects without resting wall-motion abnormalities (WMA) as detected by DSE. Measurement of LA volume was done at rest and at peak DSE, concluded that In { measurement of LAVI at peak DSE can be of great value for expectation of angiographically significant CAD high specificity and with acceptable sensitivity. In addition it can be expected multivessel CAD with high specificity and sensitivity }.

Conclusion and Recommendations:-

We concluded that LAVI is a very valuable, readily available and practical way of screening for low risk IHD patients.

In many centers, the sophisticated stress echocardiography tests might not be readily available, and hence LAVI, a procedure we recommend, should be implemented as part of work-up for the diagnosis of IHD.

Study Limitations:

Our findings are based on a relatively slight number of samples. We in need to apply this study with the same technique in multicenters to justify on the end conclusion.

Furthermore, the current work participated subjects with no resting wall motion abnormalities and patients with previously diagnosed CAD were excluded. So, it is hard to generalize our findings to patients was previously complained from myocardial infarction, or baseline resting wall motion abnormalities.

Moreover, follow-up of the patient condition for long period is necessary to clarify the prognostic value of LAVI to expect occurrence adverse cardiac events.

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